Herbal Drugs in Mirror of Alzheimer's Disease

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COMMENT

Oxidative stresses and dys-homeostasis of metal metabolism, especially Cu and Zn, in association with intracellular protein-misfolding processes of amyloid beta (Aβ) peptides, are major hallmarks in the brains of Alzheimer patients.[1] Currently, no medications for etiological treatments of Alzheimer's disease (AD), implying the recovery and modulation of metal ion homeostasis inside the cell, are so far available. Several therapeutic strategies and nearly all medications used or suggested, aim at the treatment of AD symptoms only and are not focused on the origin of this cureless chronically progressive neurodegenerative disease.[1]

The medical community, including the pharmaceutical industry, as well as AD patients have become aware of the well-known antioxidant effects of ancient herbal medications, e.g., *Ginkgo biloba* leaf extracts.[2] The mechanisms of action are thought to reflect the action of their major biologically active compounds, namely flavonoids and terpenoids. Exemplary, the flavonol quercetin was found to interact with Cu^{2+} and Fe^{3+} ions.[3] However, it is evident that commercially available medicinal plant extracts have no predictable and clinically significant benefit for people with dementia or cognitive impairment.[2] Furthermore, the results from the study of He and colleagues suggested that high doses of herbal remedies can even be toxic to cells.[4]

Thus *Ginkgo biloba* extracts may induce unwanted side-effects and may also lack specificity as to the binding of Cu^{+} and Zn^{2+} ions in the cytoplasm.[3-5] These extracts can neither reduce metal-based oxidative stress nor contribute to the homeostatic control of those metal ions in human cells. Yet, for the recovery and modulation of metal ion homeostasis in the treatment of Alzheimer's disease, we have proposed another class of pharmacologically active plant ingredients as antioxidant: plant copper chaperones for superoxide dismutase (pCCS).[5,6] These proteins have the ability to bind and deliver Cu^{+} ions specifically and to normalize Cu/Zn superoxide dismutase activity via specific protein-protein interactions in the brain and body of AD patients.[5,6] We have begun to evaluate the relative biochemical impact of pCCS in patients and probands using state-of-the-art biochemical techniques.[5,6] We believe that this promising approach might provide fundamental understanding of the complex physiological processes that may lead to oxidative stresses in protein-misfolding diseases and help to develop a novel generation of herbal drugs for Alzheimer's disease.

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